REMARKS

Reconsideration and continuing examination of the above-identified application are respectfully requested in view of the amendments above and the discussion that follows.

Claims 29 and 40 have been amended. The Action noted that claims 1-3, 6, 8-14, 18-21, 26-28, 31-36, 41 and 42 are allowable, and that claim 39 was objected to as depending from a rejected base claim. Claims 1-3, 6, 8-14, 18-22, 26-29 and 31-42 are in the case and are before the Examiner. Those claims are attached hereto. Withdrawl of the previous rejections is noted with appreciation.

I. Housekeeping Matters

A. Power of Attorney

It is noted that a Revocation and Power of Attorney document was filed with the prior Reply, and that the Action was nevertheless forwarded to the prior counsel instead to the undersigned. That mis-mailing caused a loss of time in getting the Action to counsel and his client, and the subsequent preparation of this Reply. The Examiner's assistance in seeing to the proper addressing of the next paper will be appreciated.

B. Claim 22

The previous Reply mailed November 7, 2002, noted that claim 22 was excluded from the list of pending claims in the Action to which that Reply was directed, and asserted that claim 22 should be among the pending claims. The present Action continued the omission of claim 22 as a pending claim.

A review of the Decision on Appeal indicates that claim 22 was among the claims to which that decision applied. Counsel's review of his files does not indicate cancellation of that claim. It is therefore requested that the Examiner review her files and contact the undersigned by phone if claim 22 has been cancelled. If she finds that claim 22 has not been cancelled, it is requested that the nest Action so indicate and that that claim should be allowable inasmuch as it ultimately depends from an allowed independent claim, claim 18.

II. The Amendments

Claim 29 has been amended to recite that the nucleic acid encoding a TNF-α is operatively linked to an Egr-1 promoter. This amendment is supported by the specification at least, for example, page 16, lines 1-3, and Example VI.

Claim 40 has been amended to refer to a "total" ionizing radiation dose of 50-70 Gray. This amendment is supported in the specification at least, for example, page 42, lines 19-21.

It is thus seen that no new matter has been added by these amendments.

III. Rejections Under 35 U.S.C. §112, First Paragraph

Claims 38 and 40 were rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking a written description, in that the specification was said not to specify a dose of radiation between 50 and 70 gray as set forth in claim 40. It is respectfully submitted that Example VI of the present application discloses "[t]umors will be irradiated on five

succeeding days, generally Monday through Friday, at 2 Gy/day to a total dose of 50 to 70 Gy" (see page 42, lines 19-21). Thus, the subject matter of claim is adequately described in the specification to convey to one of ordinary skill in the art that Applicants had possession of the invention. Accordingly, it is submitted that the Section 112, first paragraph rejection should be withdrawn as to claim 40.

The basis for the rejection of claim 38 under 35 U.S.C. §112, first paragraph, is not understood as that claim depends from claim 29 and does not recite a radiation dosage as does claim 40. In addition, the basis for that claim was recited in the previous Reply as being in the specification and several enumerated claims.

The Court noted in *In re Oetiker*, 977 F.2d 1443, 1445 24 USPQ2d 1443, 1444 (Fed. Cir. 1992), that the examiner "bears the initial burden . . . of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." Here, there has only been an assertion of a lack of description. It is submitted that the required burden for a rejection under 35 U.S.C. §112, first paragraph, has not been met by the unsupported assertion of the present Action in that the lack of description has not been made with the particularity as to evidence or reasons that are required under the holdings of *Oetiker*.

It is therefore submitted that the rejection should be withdrawn as claim 38 is properly supported. If this rejection is maintained, it is submitted that the present final rejection be replaced by a further action, and the time for response be

reset in view of the lack of specificity with which the rejection was made.

IV. Rejections Under 35 U.S.C. §102(e)

Claims 29 and its dependent claim, 37, were rejected together and singly under §102(e) as allegedly being anticipated by the disclosures of one or both of U.S. Patents No. 5,935,935 (the '935 patent; claims 29 and 37) and No. 6,228,356 (the '356 patent; claim 29). In particular, the Action alleges that the '935 patent and the '636 patent each disclose an adenoviral vector particle that can encode a therapeutic agent or cytokine, such as TNF-α, which can be administered to a patient in combination with a pharmaceutically-acceptable carrier. The Office Action further contends that the adenoviral vector disclosed in the '935 patent can be deficient in the E1 region and the E3 region of the adenoviral genome. These bases for rejection are respectfully traversed.

Claims 29 and 37 as amended, is directed to a pharmaceutical composition comprising a genetic construct packaged within an adenovirus particle that is dispersed in a pharmacologically acceptable carrier, in which the genetic construct comprises an Egr-1 promoter that is operatively linked to nucleic acid encoding a TNF-α. It is submitted that neither the '935 patent nor the '356 patent discloses or suggests genetic constructs comprising a TNF-α operatively linked to an Egr-1 promoter, much less an adenovirus containing such genetic constructs. As such, claims 29 and 37 define novel, as well as unobvious, subject matter in view of the '935 patent and the

'356 patent. Accordingly, withdrawal of the Section 102(e) rejections is respectfully requested.

V. Rejections Under 35 U.S.C. §103

The Office Action has rejected claims 29 and 37 under Section 103 for allegedly being unpatentable over U.S. Patent 6,143,290 ("the '290 patent") in view of Walther et al. (hereinafter Walther), *Anticancer Res.*, *13*, 1565-1574 (1993). Specifically, the Office Action contends that it would have been obvious to one of ordinary skill in the art to modify the p53-encoding adenovirus disclosed in the '290 patent and the TNF-α-encoding retrovirus disclosed in the Walther paper to arrive at the invention set forth in claim 29, particularly in view of the advantages of adenoviral vectors disclosed in the '290 patent.

The Action admits that the '290 patent teaches the use of a gene encoding the p53 protein and not a TNF-α, and quotes from a section of that patent teachings about the deficiencies in using a retroviral vector. The Walther paper teaches the use of retroviral vectors for expressing TNF-α, and used polybrene (page 1566, left column) in a composition to transfect cells *in vitro*, with those cells ultimately being placed into an animal to assess tumor growth. This basis for rejection cannot be agreed with and is respectfully traversed.

As noted before, claim 29 recites a composition comprising a genetic construct packaged within an adenovirus particle that is dispersed in a pharmacologically acceptable carrier, in which the genetic construct comprises an Egr-1 promoter that is operatively linked to nucleic acid encoding a

TNF-α. Neither the '290 patent nor the Walther paper discloses or suggests the use of an Egr-1 promoter to regulate expression of a transgene in a viral vector. Thus, claim 29, and claim 37 depending therefrom, is directed to an unobvious, as well as novel, subject matter in view of the prior art, and the Section 103 rejection should be withdrawn.

Still further, it is noted that there is no direction in the relied-upon art that teaches the skilled worker which portions of the individual disclosures one should discard in trying to make the disclosures add up to that claimed here. Thus, for example, it is submitted that only after reading the present disclosure would one know to discard the retroviral vector and use the adenovirus. One would also not know without reading this disclosure that cells were not to be transfected *ex vivo* as done in Walther, nor would that skilled worker know that a pharmacologically acceptable carrier was to be used instead of a composition containing a heparin antagonist such as polybrene. It is further submitted that there is no teaching in either relied-on disclosure that directs the skilled worker to not use the p53 protein and use a TNF-α in its place. When those deficiencies are added to the complete absence of a disclosure concerning the Egr-1 promoter in either, one sees that there is neither direction for the skilled worker, nor are there enough elements that can be summed to arrive at the present claims.

It is respectfully submitted that the present Action has used a hindsight reconstruction to go through the art and select what might be useful to try to obtain sufficient claim elements that fit with the disclosure, while discarding those teachings that do not fit. It is further submitted that the law

regarding obviousness requires more. As the CCPA held in *In re Wesslau* 147 USPQ 391, 393 (CCPA 1965)

> [i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

It is again therefore submitted that this rejection should further be withdrawn.

VI. Summary

Claims 29 and 40 have been amended. Each basis for rejection has been dealt with and made moot or otherwise overcome.

It is therefore believed that the application is in condition for allowance. An early notice to that effect is earnestly solicited.

No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be a required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,

By _____
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CERTIFICATE OF MAILING

I hereby certify that this Reply, is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Box AF, Washington, D.C. 20231 on March 28, 2003.

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Edward P. Gamson